

Imaging the Biomechanical Properties of Articular Cartilage

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Function: The primary function of articular cartilage is mechanical: under load it must deform to distribute the load over a larger area so as to minimize stress in the underlying bone. In addition, articular cartilage must provide a very low friction surface for gliding when the joint is flexed so that articulating joints move freely. Lastly, it must carry out these two functions for a lifetime of use. Understanding the biomechanics of articular cartilage is important as it provides insight into the deterioration occurring in osteoarthritis and other degenerative diseases of joints.

Organization and Composition. Articular cartilage is neither vascularized nor enervated. Chondrocytes represent a small fraction of cartilage volume as the vast majority of the tissue consists of extracellular matrix produced by the chondrocytes. This matrix is primarily comprised of two types of molecules: collagen and glycosaminoglycan (1). Collagen in the type II form is organized into fibrils which form larger diameter fibers. The fibers are anchored in the bone and stretch upwards arching throughout the cartilage layer. Proteoglycans are large molecular weight macromolecules consisting of a protein backbone (hyaluranan) with numerous glycosaminoglycans (keratin- and chondroitin- sulphate) radiating outward from it much the way the bristles on a bottle brush radiate out along the length of the brush. These glycosaminoglycans are negatively charged and attract sodium and hence water so that the interstitial space in the cartilage is highly hydrated (~75%). Collagen and proteoglycans represents respectively approximately 75% and 10-25% by dry weight of the tissue. There are large spatial variations in the architecture and composition of articular cartilage. Traditionally, articular cartilage is divided into three zones or layers: the deep zone (DZ) adjacent to the cortical bone, the middle zone (MZ) comprising the majority of the thickness of the cartilage, and a very narrow zone near the surface called the superficial zone (SZ)(2). In the DZ the collagen fibrils radiate perpendicularly upward from the cortical surface. In the MZ the orientation is more random as the collagen begins to bend away from the perpendicular. At the SZ the fibrils are oriented parallel to the surface. There is a tendency for the majority of the fibers to run in the direction of greatest stress. The concentration of PG also varies spatially being greatest in the MZ and least at the SZ. The hydration level is least (40-60%) in the DZ and rises with height in the cartilage to approximately 85% at the surface. That the tissue is highly hydrated gives it a resiliency to compression.

Basic Mechanical Properties: Extensive tensile and compressive studies have been carried out on articular cartilage from various species, at various ages of animal, and in various conditions. The tensile measurements show that the collagen fibers contribute most significantly to the tensile properties of the tissue. For example, degrading the bonds between collagen fibrils with elastase reduces the tensile modulus by over 90%. The tensile modulus is on the order of 5 – 25 MPa: higher at the surface than deeper and higher in weight bearing regions than elsewhere. Measurements of the compressive modulus of the tissue reveal that the PG contributes most significantly. There is an equilibrium between the tensile strain in the fibers and the hydrostatic pressure induced by the high concentration of water (3). The initiation of osteoarthritis (OA) leads to breaking of the collagen fibrils resulting in swelling of the tissue because the constraining effect of the collagen has been removed. This condition is detectable as a softening of the tissue which orthopedic surgeons detect by prodding the surface. Because of the

preferential orientation of the collagen parallel to the surface in the SZ the tensile properties here are higher than in the MZ. The tensile modulus can drop by an order of magnitude with disease. Compression of cartilage leads to exudation and redistribution of water through the extracellular matrix. The viscous drag caused by the porous matrix leads to creep and stress relaxation (4). Under an oscillating load the viscous drag of fluid redistribution leads to dissipation of energy.

Non-imaging Investigations of Cartilage Biomechanics: Traditional ways of investigating the biomechanical properties of articular cartilage. Material properties of articular cartilage have, for the most part, been investigated on ex vivo samples of cartilage (5). In some cases, samples of cartilage were excised from the bone and in other cases the measurement were made on intact joints or by compressing cored samples. The tensile modulus of cartilage (E) can be measured from the slope of the stress (Force/Area) versus strain ($\epsilon = \Delta L/L_0$) curve ($E = \sigma/\epsilon$) as shown in figure 1. The compressive modulus (H_A) is obtainable from indentation tests performed with a permeable indenter which allows fluid to flow out of the cartilage and through the indenter. Theoretically, the mechanical properties of articular cartilage are well described by a multiphasic viscoelastic model developed by Van Mow and others (2). This model describes the complex interaction of PGs, collagen fibers and viscous flow of the interstitial fluid to develop cartilage's impressive biomechanical features.

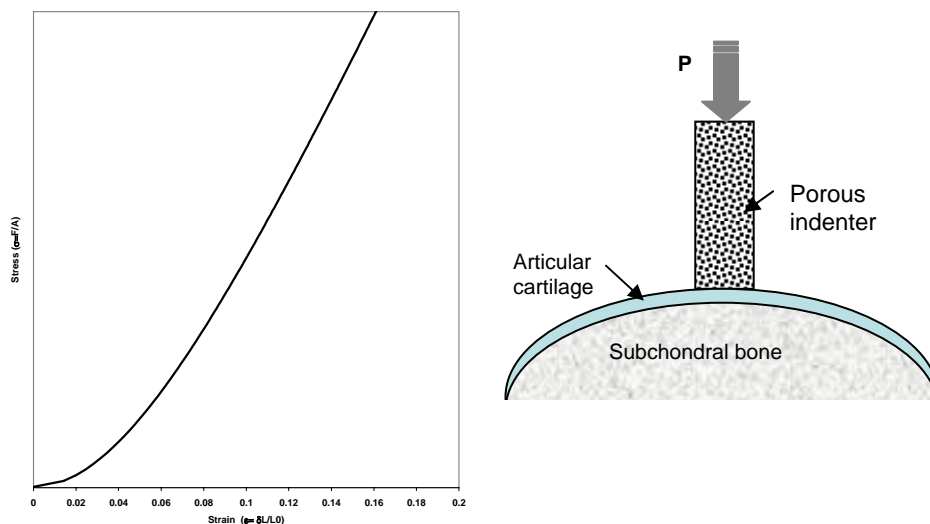


Figure 1. (left) Measurement of the tensile modulus from the stress vs strain curve. Figure 2 (right) method of carrying out indentation test to measure the compressive modulus of articular cartilage.

Imaging Method of Measuring Biomechanical Features: In one approach, MR images of cartilage have been acquired to measure various MR properties such as T1, T2 or magnetization transfer and these properties were related to mechanical measurements acquired using standard approaches (6,7). Alternatively, multiple methods have been developed employing MR imaging to measure the biomechanical properties of articular cartilage. Ekstein et al developed a pneumatic device to compress the patella against the trochlear cartilage in a cadaver knee (8,9). With this device they measured the cartilage deformation as a function of time. A few groups have developed apparatus and imaging techniques to measure the biomechanical properties of excised samples. Rubenstein et al imaged excised plugs from bovine knees under compression

to 4 MPa. They identified the layers in the cartilage and their transformation under compression both with the load and duration of compression (10). Changes in the appearance of the zones were attributed to interstitial fluid redistribution and collagen fiber reorientation. The technique was useful in understanding the origin of H_A at different stages of compression. Kaufman et al developed a pneumatic device to compress samples of articular cartilage and image them under compression. They measured the creep deformation of healthy and trypsin digested bovine calf articular cartilage samples as a function of time and found the creep was explained by a viscoelastic model(11). Neu and Hull imaged cartilage samples while cyclically loading them. They visualized the compression using tagging methods which give a direct visualization of the tissue deformation (12). Hardy et al also made measurements on excised bovine cartilage samples. They used a phase contrast method to measure the local displacement of cartilage under cyclic loading. The method is very sensitive to small deformations and can visualize strain over the entire sample(13). Both the methods of Neu and Hardy require repeated loading of the sample and the measurement of parameters once a steady state of load and compression has developed. Measurements of the elastic modulus of cartilage have also been made with the harmonic elastographic method (14). The large H_A of cartilage compared to soft tissue means the wavelength of the shear waves is much longer than the dimensions of the sample for typical elastographic frequencies of 100 – 500 Hz. To overcome this Lopez et al at Mayo constructed a dedicated gradient system which could generate large amplitude gradients (>100 mT/m) and oscillate them in excess of 1 kHz (15). However, using this apparatus they obtained measurements of the shear modulus similar to those obtained with other techniques.

Besides MR imaging a variety of other imaging techniques have been employed to measure mechanical properties of articular cartilage. Ultrasound techniques have been employed to measure the surface roughness and the deformation of cartilage under load. Kiviranta & Jurvelin have developed an orthoscopic ultrasound probe to measure the deformation and local mechanical properties of articular cartilage during orthoscopic surgery (7,11,16). This technique is especially interesting because it could be applied clinically although with specialized equipment. Even, atomic force microscopy has been recruited to study this interesting tissue. Stolz et al used AFM to examine the dynamic elastic modulus of porcine femoral articular cartilage at micro- and nano-meter scales and demonstrated variation in the dynamic elastic modulus with scale and with enzymatic degradation of collagen and proteoglycan moieties (16).

Conclusion: The mechanical properties of articular cartilage vary spatially. Thus measurements on intact samples will be aggregate measurements and will obscure the contributions from the individual layers which give cartilage its complex biomechanical behavior. To measure the properties in the individual layers by excising specific sections of tissue distorts the measurement because the collagen fibrils are severed and because new surfaces not present in the intact tissue become available for exudation of interstitial fluid. MR imaging provides several advantages for studying the biomechanical properties of tissue. MRI provides detailed measurements of the strain throughout a sample. This can be very important for understanding the contribution of each zone to the biomechanical properties of the intact tissue. In addition, it may be feasible to extend the techniques so that measurements might be made in vivo allowing the measurement of the mechanical properties of diseased tissue as a function of the course of the disease or with treatment. MRI is the ideal format to realize this tantalizing possibility.

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